WEST Search History

DATE: Friday, June 13, 2003

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ			
L9	L7 same l1	1	L9
L8	L7 same l1	1	L8
L7	l3 with l2	726	L7
L6	L5 same l1	1	L6
L5	L4 with l2	5	L5
L4	nef with vpr	288	L4
L3	auxiliary	453781	L3
L2	gutless or deficient or lack	321777	L2
L1	retrovi$ or HIV	57485	L1

END OF SEARCH HISTORY

L9 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2002 ACS
AN 2001:224379 CAPLUS
DN 134:247955
TI Improved lentiviral vectors for packaging and transduction for long-term expression in dividing and non-dividing cells
IN Chang, Lung-ji
PA USA
SO U.S., 58 pp., Cont.-in-part of U.S. Ser. No. 848,760.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6207455	B1	20010327	US 1997-935312	19970922
	US 6248721	B1	20010619	US 1997-848760	19970501
	WO 2000000600	A2	20000106	WO 1999-US11516	19990526
	WO 2000000600	A3	20001012		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI	US 1997-848760	A2	19970501
	US 1997-838702	A2	19970409
	US 1997-935312	A2	19970922
	US 1998-86635P	P	19980526

AB The present invention contemplates novel improved lentiviral vectors for the expression of genes at high levels in human and other cells. Vectors are provided which are packaged efficiently in packaging cells and cell lines to generate high titer recombinant virus stocks. The improved vectors contain novel packaging signals, an internal promoter, and a recombinant Rous sarcoma virus splicing signal. The viral gene expression vectors (pHP) were constructed to contain minimal amts. of HIV sequences, allowing efficient expression of viral structural proteins but not genome packaging. The transducing vectors (pTV) were constructed to contain all of the sequences to allow efficient genome packaging and internal promoter, but contain no viral genes and minimize the possibility of recombination with pHP. These two series of vectors demonstrated efficient gene transduction and high levels of long-term expression in many types dividing and non-dividing cells. The present invention further relates to HIV vaccines and compns. for gene therapy. In particular, the present invention provides attenuated replication-competent HIV vaccines and replication-defective HIV vectors.

L9 ANSWER 10 OF 25 MEDLINE
AN 1999214352 MEDLINE
DN 99214352 PubMed ID: 10196309
TI An intact TAR element and cytoplasmic localization are necessary for efficient packaging of human immunodeficiency virus type 1 genomic RNA.
AU Helga-Maria C; Hammarskjold M L; Rekosh D
CS Myles H. Thaler Center for AIDS and Human Retrovirus Research and Department of Microbiology, University of Virginia, Charlottesville, Virginia 22908, USA.
NC AI34721 (NIAID)
AI38186 (NIAID)
SO JOURNAL OF VIROLOGY, (1999 May) 73 (5) 4127-35.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199905
ED Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990519
AB Although most reports defining the human immunodeficiency virus type 1 (HIV-1) genomic RNA packaging signal have focused on the region downstream of the major 5' splice site, others have suggested that sequences upstream of the splice site may also play an important role. In this study we have directly examined the role played by the HIV-1 TAR region in RNA packaging. For these experiments we used a proviral expression system that is largely independent of **Tat** for transcriptional activation. This allowed us to create constructs that efficiently expressed RNAs carrying mutations in TAR and to determine the ability of these RNAs to be packaged. Our results indicate that loss of sequences in TAR significantly reduce the ability of a viral RNA to be packaged. The requirement for TAR sequences in RNA packaging was further examined by using a series of missense mutations positioned throughout the entire TAR structure. TAR mutations previously shown to influence **Tat** transactivation, such as G31U in the upper loop region or UCU to AAG in the bulge (nucleotides [nt] 22 to 24), failed to have any effect on RNA packaging. Mutations which **disrupted** the portion of the TAR stem immediately below the bulge also had little effect. In contrast, dramatic effects on RNA packaging were observed with constructs containing mutations in the lower portion of the TAR stem. Point mutations which altered nt 5 to 9, 10 to 15, 44 to 49, or 50 to 54 all reduced RNA packaging 11- to 25-fold. However, compensatory double mutations which restored the stem structure were able to restore packaging. These results indicate that an intact lower stem structure, rather than a specific sequence, is required for RNA packaging. Our results also showed that RNA molecules retained within the nucleus cannot be packaged, unless they are transported to the cytoplasm by either Rev/Rev response element or the Mason-Pfizer monkey virus constitutive transport element.

L9 ANSWER 14 OF 25 BIOTECHDS COPYRIGHT 2002 THOMSON DERWENT AND ISI
AN 1998-01556 BIOTECHDS
TI Minimal requirement for a lenti virus vector based on human immunodeficiency virus type 1;
HIV virus-1 vector construction by plasmid pHZ series, plasmid pGP series and plasmid pRV67 co-transduction of 293T cell and potential of the virus for AIDS gene therapy
AU Narry Kim V; Mitrophanous K; Kingsman S M; Kingsman A J
CS Univ.Oxford; Oxford-BioMedica
LO Biochemistry Department, Oxford University, South Parks Road, Oxford, OX1 3QU, UK.
Email: akingsmn@bioch.ox.ac.uk
SO J.Virol.; (1998) 72, 1, 811-16
CODEN: JOVIAM ISSN: 0022-538X
DT Journal
LA English
AB The use of HIV virus vectors for gene therapy is hindered by safety concerns. A minimal vector system that is capable of transducing nondividing cells and which does not contain **tat**, vif, vpr, vpu and nef, is described. The HIV virus-1 vectors were designed to be produced from transient 3-plasmid cotransfection into 293T cells. The vector genome, the HIV virus-1 **gag-pol** gene and the vesicular-stomatitis virus glycoprotein gene were placed on 3 separate plasmids (plasmid pHZ series, plasmid pGP series, and plasmid pRV67, respectively). This packaging system **lacked** the **accessory genes** nef, vpu and vpr and has the potential to eliminate **tat**, rev and vif. Virus was regenerated by calcium phosphate transfection of 293T cells and used for transduction. After incubation of the cells on dishes with DNA-calcium phosphate precipitates for 12 hr, the medium was replaced with 2.5 ml fresh medium and incubated for 36 hr. The supernatant was used for transduction in the presence of Polybrene (8 ug/ul). No replication-competent virus from the packaging system was detected after 51 days of culture. (59 ref)

L9 ANSWER 25 OF 25 MEDLINE DUPLICATE 9
AN 86175031 MEDLINE
DN 86175031 PubMed ID: 3007995
TI The trans-activator gene of HTLV-III is essential for virus replication.
AU Fisher A G; Feinberg M B; Josephs S F; Harper M E; Marselle L M; Reyes G; Gonda M A; Aldovini A; Debouk C; Gallo R C; +
SO NATURE, (1986 Mar 27-Apr 2) 320 (6060) 367-71.
Journal code: 0410462. ISSN: 0028-0836.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 198605
ED Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860507
AB Studies of the genomic structure of human T-lymphotropic virus type III (HTLV-III) and related viruses, implicated as the causal agent of acquired immune deficiency syndrome (AIDS), have identified a sixth open reading frame in addition to the five previously known within the genome (**gag**, **pol**, sor, env and 3'orf). This gene, called **tat**-III, lies between the sor and env genes and is able to mediate activation, in a trans configuration, of the genes linked to HTLV-III long terminal repeat (LTR) sequences. We now present evidence that the product of **tat**-III is an absolute requirement for virus expression. We show that derivatives of a biologically competent molecular clone of HTLV-III, in which the **tat**-III gene is **deleted** or the normal splicing abrogated, failed to produce or expressed unusually low levels of virus, respectively, when transfected into T-cell cultures. The capacity of these **tat**-III-defective genomes was transiently restored by co-transfection of a plasmid clone containing a functional **tat**-III gene or by introducing the **TAT**-III protein itself. As HTLV-III and related viruses are the presumed causal agents of AIDS and associated conditions, the observation that **tat**-III is critical for HTLV-III replication has important clinical implications, and suggests that specific inhibition of the activity of **tat**-III could be a novel and effective therapeutic approach to the treatment of AIDS.

L10 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2002 ACS
AN 2002:320878 CAPLUS
TI **HIV vaccine** strategies
AU Nabel, Gary J.
CS Vaccine Research Center, NIAID, National Institute of Health, Bethesda, MD, 20892-3005, USA
SO Vaccine (2002), 20(15), 1945-1947
CODEN: VACCDE; ISSN: 0264-410X
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
AB Traditional methods of **vaccine** development have not produced effective vaccines for several prevalent infectious diseases, including AIDS, malaria and tuberculosis. These difficult diseases call attention to the importance of new approaches that profit from modern technologies. Successful efforts in the past have typically taken advantage of naturally occurring, protective immune responses, but this avenue is not readily available in certain cases, such as in **HIV** infection, where the immune system rarely confers protective immunity. However, there are alternative strategies and areas of research that may facilitate the development of highly effective vaccines. These include the identification of immunogens that elicit broadly neutralizing antibodies, detn. of the mol. and cellular basis for immune responses to the components of the infectious agent, the identification of relevant forms of viral proteins for antigen presentation, stimulation of relevant T-cell types, and enhancement of antigen-presenting, dendritic cell function. Answering these basic research questions will aid in rational **vaccine** design. It is also extremely important to optimize techniques for the testing and prodn. of new vaccines including the quantitation of immune responses in animals and in humans, identification of surrogate markers of immune protection, streamlined **vaccine** prodn., and rapid evaluation of candidate vaccines for testing in clin. trials. We have put these ideas into practice in two recent studies in which we generated enhanced cytotoxic T lymphocyte (CTL) responses, while retaining robust humoral responses, to wild-type viral proteins by immunizing mice with genetically modified forms of **HIV**-1 Env, Gag and Pol delivered in the form of **plasmid** DNA expression

L10 ANSWER 6 OF 20 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
AN 2001406109 EMBASE
TI Nucleic acid vaccines: Tasks and tactics.
AU McKenzie B.S.; Corbett A.J.; Brady J.L.; Dyer C.M.; Strugnell R.A.; Kent S.J.; Kramer D.R.; Boyle J.S.; Lew A.M.
CS Dr. A.M. Lew, WEHI, P.O. RMH, Parkville, Vic. 3050, Australia. lew@wehi.edu.au
SO Immunologic Research, (2001) 24/3 (225-244).
Refs: 191
ISSN: 0257-277X CODEN: IMRSEB
CY United States
DT Journal; General Review
FS 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LA English
SL English
AB There are no adequate vaccines against some of the new or reemerged infectious scourges such as **HIV** and TB. They may require strong and enduring cell-mediated immunity to be elicited. This is quite a task, as the only known basis of protection by current commercial vaccines is antibody. As DNA or RNA vaccines may induce both cell-mediated and humoral immunity, great interest has been shown in them. However, doubt remains whether their efficacy will suffice for their clinical realization. We look at the various tactics to increase the potency of nucleic acid vaccines and divided them broadly under those affecting delivery and those affecting immune induction. For delivery, we have considered ways of improving uptake and the use of bacterial, replicon or viral vectors. For immune induction, we considered aspects of immunostimulatory CpG motifs, coinjection of cytokines or costimulators and alterations of the antigen, its cellular localization and its anatomical localization including the use of ligand-targeting to lymphoid tissue. We also thought that mucosal application of DNA deserved a separate section. In this **review**, we have taken the liberty to discuss these enhancement methods, whenever possible, in the context of the underlying mechanisms that might argue for or against these strategies.

L10 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2
AN 1998:426180 CAPLUS
DN 129:201753
TI DNA vaccines: a **review** of developments
AU Webster, Robert G.; Robinson, Harriet L.
CS Department of Virology and Molecular Biology, St. Jude Children's Research Hospital, Memphis, TN, USA
SO BioDrugs (1997), 8(4), 273-292
CODEN: BIDRF4; ISSN: 1173-8804
PB Adis International Ltd.
DT Journal; General Review
LA English
AB A **review** with 110 refs. Immunization with purified DNA is a powerful technique for inducing immune responses. The concept is very simple, involving insertion of the gene encoding the antigen of choice into a bacterial **plasmid**, and injection of the **plasmid** into the host where the antigen is expressed and induces humoral and cellular immunity. This technol. can induce immunity to all antigens that can be encoded by DNA; this includes all protein, but not carbohydrate, antigens. DNA immunization appears to result in presentation of antigens to the host's immune system in a natural form, similar to that achieved with live attenuated vaccines. The most efficacious routes for DNA immunization are bombardment with particles coated with DNA (gene-gun), followed by i.m. and intradermal administration. The efficiency of transfection of host cells is low, but sufficient to induce immunol. responsiveness. The DNA **plasmid** is retained in the transfected cells in an unintegrated form for the life of the cell. The majority of transfected cells are eliminated, but residual expression has been detected for longer periods. In animal model systems, DNA immunization has been shown to induce protective immunity to influenza, herpes, rabies, hepatitis B and lymphocytic choriomeningitis viruses, and to malaria and mycobacteria. However, strategies to induce protective immunity to **HIV** and other disease agents remain to be developed. DNA vaccines permit modulation of the immune response by altering the route or method of DNA administration, by including immunostimulatory sequences in the **plasmid**, and by co-administration of cytokine genes with the gene encoding the antigen of interest. A T helper 1 response provides cell-mediated immune killing of infected cells and neutralizing antibody prodn., while a T helper 2 response induces IgE and allergic responses. The advantages of DNA immunization are: (i) similarity to live attenuated vaccination but without the possibility of contamination with undesirable agents; (ii) correct presentation of antigen; (iii) combinations of DNA-encoded antigens and/or cytokines may be administered; (i.v.) genetic stability; (v) potential speed of making new vaccines with genetic identity; (vi) development of vaccines for agents that cannot be grown in culture; (vii) no need for a cold chain; and (viii) possibility of modulation of the immune response. The perceived risks include: (i) integration of the **plasmid** into the host genome; (ii) induction of anti-DNA antibodies and autoimmunity; and (iii) induction of tolerance. The available information concerning safety is encouraging, with the risk of integration being considered to be orders of magnitude below the spontaneous mutation frequency in humans. DNA immunization offers the possibility of extending the control of infectious diseases far beyond those that are currently controlled by conventional and recombinant vaccines, to include vaccines for parasites and cancer. However, it is currently too early to predict the future extent of use of DNA vaccines in human immunization programs because the initial clin. trials are still in progress.